

### **IN THE SPECIFICATION**

Please replace the first full paragraph at page 1, lines 4-11, with the following:

The present application is a continuation of United States Application Serial No. 08/738,947, filed October 24, 1996, now allowed, which is a continuation-in-part of ~~co-pending~~ United States Patent Application Serial No. 08/462,350, filed June 5, 1995, now abandoned, which is a continuation-in-part of ~~co-pending~~ United States Patent Application Serial No. 08/243,342, filed May 16, 1994, now abandoned which is a continuation-in-part of United States Patent Application Serial No. 08/063,399, filed May 17, 1993 (now abandoned), each of which is incorporated herein by reference ~~herein-in its~~ in their entirety.

Replace the second paragraph at page 5, lines 12-21, with the following:

Figure 5. Inhibition of Proliferation of Human Endothelial Cells In Vitro With MIF Antisense Oligonucleotides. Proliferating human microvascular endothelial cells (fourth passage; Clonetics), cultured in ECG-1 (5,000/well in a 96-well plate), were transfected with the following phosphorothionate oligonucleotides [SEQ ID NOS.: 1 and 2] (10 µg/ml; Oligo's etc.; Wilsonville, OR) using Lipofectin reagent per the manufacture's protocol (Gibco; Gaithersburg, MD):

S-MIF: 5'-GCC-ATC-ATG-CCG-ATG-TTC-AT-3' [SEQ ID NO.: 1] (SENSE, HUMAN  
MIF)

AS-MIF: 5'-ATG-AAC-ATC-GGC-ATG-ATG-GC-3' [SEQ ID NO.: 2] (ANTI-SENSE,  
HUMAN MIF).

After 16 hours, the proliferative activity of these cultures was measured over the subsequent eight hours by the incorporation of [<sup>3</sup>H]thymidine (4 μCi/ml) into DNA as measured by liquid scintillation counting.

Replace the third paragraph at page 5, line 26 through page 6, line 6, with the following:

Figure 6. Inhibition of Proliferation of Myelogenous Leukemia Cells With MIF

Antisense Oligonucleotides. Log phase proliferating K-562 chronic myelogenous leukemia cell cultures (5,000 cells/well in a 96-well plate; obtained from ATCC; Rockville, MD) were transfected with the following phosphorothionate oligonucleotides [SEQ ID NOS.: 1 and 2]

(10 μg/ml; Oligo's etc.) using Lipofectin reagent per the manufacture's protocol (Gibco):

S-MIF: 5'-GCC-ATC-ATG-CCG-ATG-TTC-AT-3' [SEQ ID NO.: 1] (SENSE, HUMAN MIF)

AS-MIF: 5'ATG-AAC-ATC-GGC-ATG-ATG-GC-3' [SEQ ID NO.: 2] (ANTI-SENSE, HUMAN MIF).

After 16 hours incubation under standard cell culture conditions (37°C, 5% CO<sub>2</sub> in humidified air atmosphere) the proliferative activity of these cultures was measured over the subsequent eight hours by the incorporation of [<sup>3</sup>H]thymidine (4 μCi/ml; DuPont) into DNA as measured by liquid scintillation counting.

Replace the third paragraph at page 19, line 33 through page 20 through line 14, with the following:

Nucleotide sequences derived from the coding, non-coding, and/or regulatory sequences of the MIF and/or MIF receptor genes may be used to prevent or reduce the expression of these genes, leading to a reduction or inhibition of MIF activity. The nucleotide sequence encoding the human MIF protein has been reported [SEQ ID NO.: 3] (see co-pending application Serial

No. 08/462,350). Further, the MIF receptor amino acid sequence provided in co-pending application Serial No. 08/462,350, may be used to design oligonucleotides for the regulation of MIF receptor genes. Among the techniques by which such regulation of gene expression may be accomplished are, as described below, antisense, triple helix, and ribozyme approaches. Administration of these nucleotide sequences, therefore, may be used to temporarily block expression and/or transcription of the MIF and/or MIF receptor genes as one method of treatment for conditions involving MIF-dependent regulation of cell growth, cell cycle, differentiation or proliferation of cell populations or tumorigenesis.

Replace the fourth paragraph at page 37, line 36 through page 38, line 24, with the following:

Proliferating human microvascular endothelial cells (fourth passage) (Clonetics; San Diego, CA) 5,000/well in a 96-well plate[[]] were incubated with 10-200  $\mu\text{g/ml}$  of IgG<sub>1</sub> Control (Sigma; St. Louis, MO) or anti-MIF neutralizing monoclonal antibody XIV.15.5 (courtesy of Dr. C. Metz, Department of Medical Biochemistry, The Picower Institute for Medical Research; Manhasset, NY) in Endothelial Cell Growth Medium containing 1% fetal bovine serum (ECG-1; Clonetics) for three hours. The proliferative activity of these cultures was measured over the subsequent 16 hours by the incorporation of [<sup>3</sup>H]thymidine (4  $\mu\text{Ci/ml}$ ) (DuPont; Boston, MA) into DNA as measured by liquid scintillation counting (FIG. 3). Proliferating human microvascular endothelial cells (fourth passage; Clonetics), cultured in ECG-1 (5,000/well in a 96-well plate), were transfected with the following phosphorothionate oligonucleotides (10  $\mu\text{g/ml}$ ; Oligo's etc.; Wilsonville, OR) using Lipofectin reagent per the manufacture's protocol (Gibco; Gaithersburg, MD):

~~S-MIF: 5'-GCC-ATTC-ATG-CCG-ATG-TTC-AT-3' [SEQ ID NO.: 1] (SENSE, HUMAN MIF)~~

S-MIF: 5'-GCC-ATC-ATG-CCG-ATG-TTC-AT-3' [SEQ ID NO.: 1] (SENSE, HUMAN MIF)

AS-MIF: 5'-ATG-AAC-ATC-GGC-ATG-ATG-GC-3' [SEQ ID NO.: 2] (ANTI-SENSE,  
HUMAN MIF).

After 16 hours, the proliferative activity of these cultures was measured over the subsequent eight hours by the incorporation of [<sup>3</sup>H]thymidine (4  $\mu$ Ci/ml; DuPont) into DNA as measured by liquid scintillation counting (FIG. 5).

Replace the second full paragraph page 39, lines 10-19, with the following:

Log phase proliferating K562 chronic myelogenous leukemia cell cultures (5,000 cells/well in a 96-well plate; obtained from ATCC; Rockville, MD) were transfected with the following phosphorothionate oligonucleotides (10  $\mu$ g/ml; Oligo's etc.) using Lipofectin reagent per the manufacture's protocol (Gibco):

~~S-MIF: 5'-GCC-ATTC-ATG-CCG-ATG-TTC-AT-3' [SEQ ID NO.: 1] (SENSE, HUMAN MIF)~~

S-MIF: 5'-GCC-ATC-ATG-CCG-ATG-TTC-AT-3' [SEQ ID NO.: 1] (SENSE, HUMAN MIF)

AS-MIF: 5'-ATG-AAC-ATC-GGC-ATG-ATG-GC-3' [SEQ ID NO.: 2] (ANTI-SENSE,  
HUMAN MIF).

After 16 hours incubation under standard cell culture conditions (37°C, 5% CO in humidified air atmosphere) the proliferative activity of these cultures was measured over the subsequent eight hours by the incorporation of [<sup>3</sup>H]thymidine (4  $\mu$ Ci/ml; DuPont) into DNA as measured by liquid scintillation counting.

Please insert the attached paper copy of the “Sequence Listing” after the last page of the specification.